

Establishment of an architecture-specific experimental validation approach for finite element modeling of bone by rapid prototyping and high resolution computed tomography

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Abstract

A new experimental validation method for assessing the accuracy of large-scale finite element (FE) models of bone micro-structure at the apparent and tissue level was developed. Augmented scaled bone replicas were built using rapid prototype machines based on micro-computed tomography (micro-CT) data. The geometric accuracy of the model was evaluated by comparing experimental tests with the replicas to the FE solution based on the same micro-CT data. A new version of the large-scale FE solver was developed to incorporate orthotropic material properties, hence the experimentally determined properties of the rapid prototype material were input into the FE models. The modified FE solver predicted the experimental apparent level stiffness within less than 1%, and the difference between experimental strain gauge measurements and FE-calculated surface stresses was 7% and 49% on a flat and curved surface region, respectively. While absolute error estimates of surface stresses were limited due to strain gauge errors, the relatively larger difference on the curved surface is indicative of the limitations of a hexahedron FE model for representing such geometries. Although the validation approach is applied here for hexahedron based meshes, the method is flexible for varying bone architectures and will be important for validation of future large-scale FE modeling developments that utilize techniques such as mesh smoothing and tetrahedron elements.

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1. Introduction

Characterization of bone mechanics is a key component for research into bone diseases such as osteoporosis, and the finite element (FE) modeling technique in combination with three-dimensional (3D) imaging methods has become an important tool for this area of research. Using computed tomography (CT), patient-specific FE models representing bone on the continuum level can be used to estimate bone strength [1], and therefore form a basis for predicting fragility

fractures. However, it is increasingly recognized that the underlying micro-architecture plays an important role in bone mechanics [2,3], therefore large-scale FE models based on high-resolution computed tomography (micro-CT) or high-resolution magnetic resonance imaging (micro-MR) have been developed [4,5] to predict apparent-level stiffness, and in some cases strength [6–8]. Furthermore, large-scale FE models provide estimates of local tissue mechanics which can give insight into the mechanisms of bone loss [9,10], as well as form a basis for inductive physiological models of mechanically driven bone adaptation [11–13]. The majority of large-scale FE models to date have focused on ex vivo analyses (i.e., biopsy or cadaver) due to resolution issues,

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however with the advent of new MR and CT technologies, patient-specific FE modeling is becoming increasingly common [8,14].

The current standard for large-scale FE meshing is based on converting each voxel in a 3D image into a hexahedron element, and this can be performed fast and efficiently representing complex bone micro-architectures [3,15], thus making it feasible to perform patient-specific FE models. The hexahedron meshes are solved using specialized FE solvers that take advantage of the fact that each element has the same (or scaled) stiffness matrix, and therefore meshes with millions of elements can be solved to produce approximations of apparent and tissue level mechanics [16,17] as computing resources permit. A known limitation of the hexahedron-based FE models is that stress raisers occur at the tissue level due to the jagged representation of smooth bone surfaces [18–20]. Addressing the magnitude of the tissue-level errors, validation to date has been based on modeling regular geometries (i.e., cylindrical shapes) and comparing the FE prediction of local stress with analytical calculations [18]. Although providing an estimation of the tissue-level errors, this approach is limited to simple geometries, loading conditions and material properties for which analytical calculations can be performed. Typical bone architectures are significantly more complex than cylinders and beams, therefore approach for validating large-scale FE models using real architectures is valuable. This has the advantage that subject-specific or bone quality specific validation can be performed, and this is particularly important for low bone mass models where mesh resolution may introduce problems. Furthermore, there is active interest in developing alternative meshing strategies based on hexahedron mesh smoothing or using different elements [15,21–24] and an experimental validation approach will be flexible for assessing these new meshing strategies and aid in the development of the large-scale FE method for non-invasive mechanical testing.

Ideally, experimental validation should be performed on the same bone architecture modeled with the large-scale FE method. However, it is not feasible to measure local strain on tissue micro-architecture due to the small sizes of the trabeculae (i.e., $<200\ \mu\text{m}$). Alternatively, with high-resolution measurements of bone architecture, it is possible to build scaled replicas of bones for experimental validation [25]. Rapid prototyping using the fused-deposition modeling (FDM) process [26] can build replicas at scales that make it possible to attach traditional strain measurement devices to the model surface. Although these replicas have different tissue properties than bone tissue, they are able to represent the complex micro-structural geometry of the original bone against which alternative meshing strategies can be tested. Currently, FE approaches focus on the effects of geometry rather than bone tissue material characteristics due to the difficulty in obtaining accurate material data.

The purpose of this study is to establish a gold standard experimental validation method for assessing the accuracy

of large-scale FE models at both the apparent and tissue levels based on bone-specific geometry. Replicas will be built by rapid prototyping based on micro-CT data, and the orthotropic material properties of the rapid prototyping material will be incorporated into a large-scale FE solver modified for that task. Testing of the validation approach is done here based on traditional hexahedron meshes, but the approach is versatile for validation of future developments in FE modeling, and for many different architectures.

2. Material and methods

The establishment of this validation tool involves multiple steps which are summarized as: (i) material property characterization of the rapid prototyping machine material matrix, (ii) construction of rapid prototype replicas from micro-CT data, (iii) development of a large-scale FE solver for orthotropic material properties, and (iv) comparison of experimental test results from replicas to the FE solution at the apparent and tissue level.

2.1. Material properties

The rapid prototyping system used in this study (FDM Titan, Stratasys Inc., Eden Prairie, MN, USA) produces parts using the fused deposition modeling (FDM) process where acrylonitrile butadiene styrene (ABS) plastic is deposited from extruded filaments with a reported spatial accuracy of $\pm 0.127\ \text{mm}$ [26]. The layer-by-layer construction results in a material matrix that is homogeneous, but transversely isotropic where the in-plane stiffness is different than the out-of-plane stiffness [27–29]. Characterization of the matrix material properties was necessary so that the FE model could accurately represent the ‘tissue’ properties. The five independent constants determined included the in-plane (E_p) and out-of-plane (E_z) elastic moduli, the in-plane shear modulus (G_{zp}), and the in-plane (ν_p) and out-of-plane (ν_{pz}) Poisson’s ratios. A preliminary test was performed to determine the sensitivity of the FDM material to strain rates and to confirm that the material exhibits a linear stress–strain region. Prismatic specimens ($N=6$; $12.7\ \text{mm} \times 12.7\ \text{mm} \times 50.8\ \text{mm}$) were subjected to uniaxial compression at rates of 0.035, 0.278 and 0.528%/s, and the corresponding stress–strain curves were determined. Subsequently, a series of experimental mechanical testing techniques was used to determine the material constants that defined the linear transversely isotropic properties (Fig. 1) as described in the following.

Prismatic test specimens ($12.7\ \text{mm} \times 12.7\ \text{mm} \times 50.80\ \text{mm}$; FDM Titan) were built for determination of the elastic moduli. Geometric accuracy and density was calculated for all specimens. Uniaxial compression was performed (TTS-25kN, Adelaide, Toronto, Canada) using a protocol designed for testing the properties of rigid plastics [30] at a strain rate of 0.33%/s, and crosshead

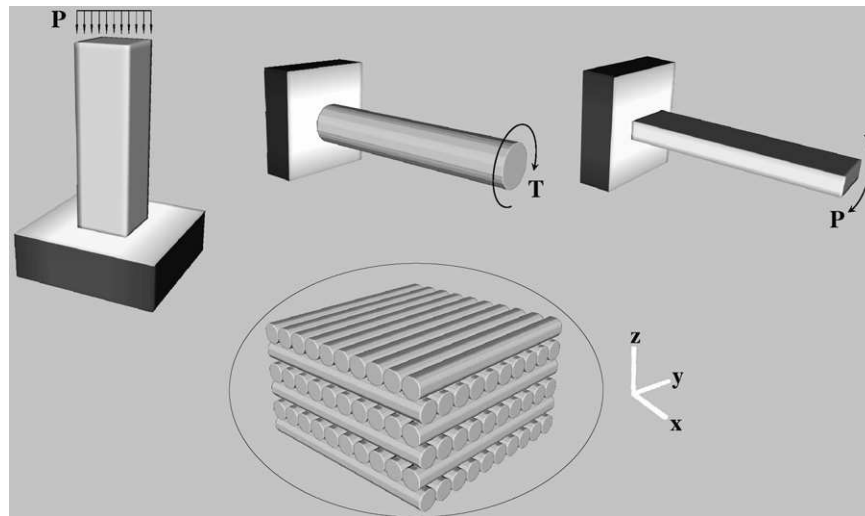


Fig. 1. The fused-deposition material built layer-by-layer results in a transversely isotropic material matrix (bottom). The in-plane material orientation is defined by the XY plane, and the out-of-plane orientation is defined by the Z axis. Compression tests were performed to determine the in-plane (E_p) and out-of-plane (E_z) elastic moduli (top left); a torsion test was performed to determine the modulus of rigidity (G_{zp} ; top middle), and bending tests were performed to determine the Poisson's ratio (ν_p and ν_{zp} ; top right).

and displacement data acquisition was recorded at 10 Hz. Specimens were oriented with the planes perpendicular to the loading direction to determine E_z ($N=3$) and aligned with the loading direction to determine E_p ($N=3$). The linear region of the stress–strain curve was used to determine the respective moduli of elasticity. Shear modulus (G_{zp}) was determined using cylindrical test specimens ($N=3$; 19.05 mm diameter, 160 mm length) built with the planes oriented perpendicular to the cylinder axis. A torsion testing machine (Torsion-1000 Mn, Tinius Olsen, Horsham, USA) with a pair of custom built jigs designed to reduce stress concentrations on the specimens was used. Twist was incremented manually in steps of 0.005 radians/mm while resultant torque was recorded, and the linear region of the torque–twist plot was used to determine the shear modulus. Finally, the Poisson's ratio was determined based on the ratio of measured strains on the top and bottom surface of a beam subjected to cantilever bending [31]. Cantilever beam specimens ($N=4$; 160 mm $\times$ 25 mm $\times$ 10 mm) were built with planes perpendicular and aligned with the length of the beam to determine to determine ν_p and ν_{zp} , respectively. Axial strain gauges (EA-06-125BT-120, Micro-measurements, Vishay Instruments, Mavern, USA) were mounted on the top and bottom surfaces with the axis aligned and perpendicular to the beam axis (offset by 90° orientation). Loads of up to 400 N were applied in increments of 50 N, and the Poisson's ratio was calculated for each load. Poisson's ratio was calculated from strain measurements ($\nu_p = \varepsilon_y/\varepsilon_x$, $\nu_{zp} = \varepsilon_y/\varepsilon_x$) and is theoretically independent of the load applied in the linear region [31]. Therefore, a single test specimen for each layer orientation provided nine estimates of Poisson's ratio. For all material constants determined, the mean and standard deviation of the experimental results were reported.

2.2. Model construction and testing

A trabecular bone core from the distal femur of a skeletally mature mixed breed dog was used for the validation model [10,32]. The bone was scanned by high resolution computed tomography (micro-CT) (μ CT 20, Scanco Medical, Bassersdorf, Switzerland) at a nominal isotropic resolution of 34 μ m, and the 3D data was Gaussian filtered ($\sigma=1.2$, finite support=2) and thresholded (11.0% of maximal possible gray value) to extract the mineralized bone phase. A sub-volume with dimensions 1.7 mm $\times$ 1.7 mm $\times$ 1.7 mm was used that included at least five trabeculae in each direction [33] resulting in 51,378 voxels representing the bone phase. The average trabecular thickness and separation of this specimen was 185 and 225 μ m, respectively, thus the average number of voxels across each trabeculae was greater than 5 [18].

The 3D micro-CT data was used as a basis to build five scaled replicas by the FDM process. A triangularized surface was generated for input to the FDM machine. An isosurface [34] was extracted using custom software such that the resulting volume matched the original data volume. Subsequently, the triangularized surface data was scaled (29.4:1) and exported (stereolithography format) such that the FDM machine could build the five replicas having dimensions 50 mm $\times$ 50 mm $\times$ 50 mm (Fig. 2). The machine settings on the rapid prototyping machine were an extrusion temperature of 290 °C, extrusion support temperature of 200 °C, layer thickness of 0.254 mm and a ± 0.127 mm accuracy. Subsequent to replica construction, the support material was dissolved leaving only the ABS structure. The volume and density of the five replicas were calculated to determine the precision and repeatability of the manufacturing process [35].

The five replicas were each instrumented with two rosette strain gauges mounted on their surfaces (EA-06-031RB-120,

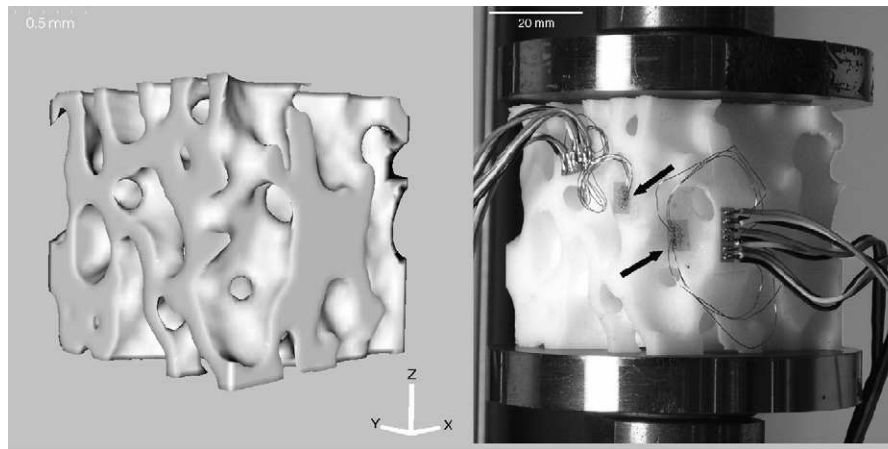


Fig. 2. The $1.7\text{ mm} \times 1.7\text{ mm} \times 1.7\text{ mm}$ micro-computed tomography scan of trabecular bone architecture (left) was used to construct a rapid prototype ($50\text{ mm} \times 50\text{ mm} \times 50\text{ mm}$) bone replica (right). Rosette strain gauges were mounted on a flat and curved surface (arrows) of the replica so that surface stress could be calculated as the specimen was subjected to uniaxial compression (platens shown).

active gauge length 0.79 mm , Micro-Measurements group, Vishay Instruments, Mavern, USA). One gauge was mounted on a flat surface and one on a concave surface at the same spatial location of each model (Fig. 2). The two surface types were deliberately chosen because the FE method has different expected errors for flat and curved surfaces, and because of differences in technical difficulty of mounting gauges on flat versus curved surfaces.

Mechanical testing was performed on each of the five instrumented FDM models. A total of 20 repeated uniaxial compression tests were performed at a strain rate of $0.33\%/s$, and lubricant was placed on the platens to reduce friction for uniaxial testing. The protocol involved five pre-conditioning loading cycles to $1\% \varepsilon$ followed by five recorded measurements. Subsequently, a second five pre-conditioning loading cycles to $2\% \varepsilon$ was performed again followed by five repeated tests. For each test, the platen displacement (corrected for compliance) and force measured by a load cell was recorded simultaneously with strain measurements from both strain rosettes mounted on the surface (Strain Indicator Calibrator 1550, Vishay Instruments, Mavern, USA). The apparent elastic modulus was calculated for each test by determining the stress–strain curve from the force–displacement data. Stress was calculated by dividing the force by the cross-sectional area (2500 mm^2), and engineering strain was calculated relative to the original side length (50 mm). From the rosette strain data, the general state of strain was determined and subsequently the state of plane stress at the surface of the replicas [36]. The first principal stress (σ_1) was used for evaluation against the FE model because this parameter is not sensitive to misalignment of the global coordinate systems between the replicas and the FE models.

The technical difficulties of mounting the rosette strain gauges on the FDM bone surfaces was a concern as gauge errors may confound the validation results. Two additional tests were performed with regular shaped FDM beams where

gauge mounting was relatively easy so that an estimate of the errors due to mounting could be approximated. Cantilever bending was applied to rectangular ($N=2$; $20\text{ mm} \times 5\text{ mm}$) and cylindrical ($N=2$; 15 mm diameter) beams, both 90 mm long. Rosette strain gauges (EA-06-062RE-120, active gauge length 1.58 mm , Micro-Measurements Group, Vishay Instruments, Mavern, USA) were mounted 50 mm from the free end of each beam, and readings were taken when the free end was displaced by 1 mm (monitored by a deflection gauge). The first principal stress was calculated from the rosette strain and compared with the FE solution of the rectangular ($500\text{ }\mu\text{m}$ isotropic element size) and cylindrical beams ($417\text{ }\mu\text{m}$ isotropic element size). Although these tests are done using regular geometries and loading conditions that do not truly represent normal trabecular loading, the tests provide insight into the relative influence of gauge mounting and FE meshing inaccuracies inherent to this validation approach. An analytical solution for each test was determined using beam theory and the simplification of an isotropic homogeneous material.

2.3. Modification of the large-scale FE solver

A pre-conditioned conjugate gradient element-by-element large-scale FE solver [37] developed previously in our laboratory [10] was modified to incorporate orthotropic properties. Due to the layer-by-layer FDM construction process, it is reasonable to assume that the material or transverse isotropy (a special sub-case of orthotropy) was oriented consistently throughout the model [27–29]. Thus, rather than incorporating a standard isotropic stiffness matrix in the FE solver representing the elastic modulus, E , and Poisson's ratio, ν , the general case of orthotropy was assumed with nine independent constants including three Young's moduli (E_1 , E_2 , E_3), three Poisson's ratios (ν_{12} , ν_{23} , ν_{31}) and three shear moduli (G_{12} , G_{23} , G_{31}), resulting in a fourth-rank stiffness tensor,

S [38]:

$$[\mathbf{S}] = \begin{bmatrix} \frac{1 - \nu_{23}\nu_{32}}{E_2 E_3 \Delta} & \frac{\nu_{21} + \nu_{31}\nu_{23}}{E_2 E_3 \Delta} & \frac{\nu_{31} + \nu_{21}\nu_{32}}{E_2 E_3 \Delta} & 0 & 0 & 0 \\ \frac{\nu_{12} + \nu_{13}\nu_{32}}{E_3 E_1 \Delta} & \frac{1 - \nu_{31}\nu_{13}}{E_3 E_1 \Delta} & \frac{\nu_{32} + \nu_{31}\nu_{12}}{E_3 E_1 \Delta} & 0 & 0 & 0 \\ \frac{\nu_{13} + \nu_{12}\nu_{23}}{E_1 E_2 \Delta} & \frac{\nu_{23} + \nu_{13}\nu_{21}}{E_1 E_2 \Delta} & \frac{1 - \nu_{12}\nu_{21}}{E_1 E_2 \Delta} & 0 & 0 & 0 \\ 0 & 0 & 0 & 2G_{12} & 0 & 0 \\ 0 & 0 & 0 & 0 & 2G_{23} & 0 \\ 0 & 0 & 0 & 0 & 0 & 2G_{31} \end{bmatrix}, \quad (1)$$

where $\Delta = (1 - \nu_{12}\nu_{21} - \nu_{23}\nu_{32} - \nu_{31}\nu_{13} - 2\nu_{12}\nu_{23}\nu_{31})/E_1 E_2 E_3$. For the special sub-case of transverse isotropy, the matrix above can be reduced to the five independent material constants (E_p , E_z , ν_p , ν_{pz} , G_{zp}) expressed as

$$[\mathbf{S}] = \begin{bmatrix} \frac{1 - \nu_{pz}\nu_{zp}}{E_p E_z \Delta} & \frac{\nu_p + \nu_{zp}\nu_{pz}}{E_p E_z \Delta} & \frac{\nu_{zp} + \nu_p\nu_{pz}}{E_p E_z \Delta} & 0 & 0 & 0 \\ \frac{\nu_p + \nu_{pz}\nu_{zp}}{E_z E_p \Delta} & \frac{1 - \nu_{zp}\nu_{pz}}{E_z E_p \Delta} & \frac{\nu_{zp} + \nu_p\nu_{pz}}{E_z E_p \Delta} & 0 & 0 & 0 \\ \frac{\nu_{pz} + \nu_p\nu_{pz}}{E_p E_p \Delta} & \frac{\nu_{pz} + \nu_{pz}\nu_p}{E_p E_p \Delta} & \frac{1 - \nu_p\nu_p}{E_p E_p \Delta} & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{E_p}{1 + \nu_p} & 0 & 0 \\ 0 & 0 & 0 & 0 & 2G_{zp} & 0 \\ 0 & 0 & 0 & 0 & 0 & 2G_{zp} \end{bmatrix}, \quad (2)$$

where $\Delta = (1 + \nu_p)(1 - \nu_p - 2\nu_{pz}\nu_{zp})/E_p^2 E_z$ and $\nu_{pz} = \nu_{zp} E_p / E_z$. The element-by-element FE solver utilized the transversely isotropic form for FE simulations of mechanical testing of the replicas.

The modified large-scale FE solver with orthotropic properties was verified using a small mesh (7087 elements) against a solution from a standard commercial software package (MSC Software Corporation, Santa Ana, USA). Both FE models were solved with identical orthotropic material properties and boundary conditions, and the element-wise von Mises stress was compared by linear regression.

2.4. FE model validation

The segmented micro-CT data used to generate the five FDM models was meshed using eight node hexahedron elements resulting in 51,378 elements and 73,383 nodes (217,417 degrees of freedom). The FE solution calculated at the eight gauss points in each element were interpolated to the element centroid. The volume of the FE mesh was calculated and compared to the replica volumes. The FE mesh was assigned transversely isotropic material properties (as per previous material test results), and uniaxial boundary conditions were imposed. Specifically, nodes on the bottom surface were constrained in the Z direction (loading axis) and free to translate in the X–Y directions, while a 2% ε was imposed in the Z direction on the top surface (X–Y unconstrained). No constraints were imposed on the lateral faces of the mesh. As noted previously, on average there were more

than five elements per trabecular width which exceeded the minimum recommendation of four necessary for FE solution convergence [18].

The apparent elastic modulus, E_a , of the FE model was calculated based on the summed nodal reaction forces in the Z direction acting over the cross-sectional area of the face (50 mm $\times$ 50 mm). These results were compared to the apparent elastic modulus of the replicas determined experimentally. The local stress was determined from the FE model at the two corresponding spatial positions as the strain gauge locations in the replicas. Nine elements representing 9 mm² surface area were averaged [18] to calculate the local stress from which the first principal stress was determined for comparison with the stress measured in the replicas. The 9 mm² surface area corresponded roughly to the area of the rosette gauges on the model surface (three gauges, each with a 0.79 mm active gauge length).

Additional FE models were developed to test the influence of the transversely isotropic, uniaxial compression assumptions based on the same meshes as above (51,378 elements and 73,383 nodes). These models were evaluated with different boundary conditions (axial versus uniaxial loading conditions) and different material properties (isotropic and transversely isotropic). Axial compression was represented with boundary conditions such that nodes on the bottom surface were constrained in the X–Y–Z directions and nodes in the top surface were constrained in the X–Y directions with a Z displacement equivalent to 2% ε . Both axial and uniaxial

FE models were solved using the transversely isotropic material properties determined in the material tests, as well as with isotropic material properties (using E_z , ν_{zp}). It was expected that the FE model with transversely isotropic material properties tested under conditions of uniaxial compression would most closely predict the experimental results.

3. Results

Compression, torsion and bending tests performed to determine the transversely isotropic material properties, in addition to the full model uniaxial compression testing for apparent and local level stress, demonstrated a linear region for the FDM material. The strain rate tests confirmed a linear elastic stress–strain relation for all three strains tested, where the limit of proportionality varied as a function of the particular strain rate above a 2% ε . Subsequently, a strain rate of 0.33%/s with an absolute strain below 2% ε was used for all tests.

The determination of the elastic moduli from the compression tests, and the modulus of rigidity from the torsion tests were based on the linear region of their respective curves (Fig. 3). The end of the non-linear toe region (com-

Table 1

The experimentally determined transversely isotropic material properties (mean and standard deviations), and the equivalent orthotropic material constants calculated for use in the modified finite element solver

Transverse isotropy		Equivalent orthotropic properties	
E_p (MPa)	1438 (15)	E_1, E_2 (MPa)	1438
E_z (MPa)	1253 (21)	E_3 (MPa)	1253
G_p (MPa)	–	G_{12} (MPa)	545
G_{zp} (MPa)	472 (14)	G_{23}, G_{31} (MPa)	472
ν_p	0.319 (0.003)	ν_{12}, ν_{21}	0.319
ν_{zp}	0.343 (0.002)	ν_{32}, ν_{31}	0.343
ν_{pz}	–	ν_{23}, ν_{13}	0.394

pression tests) and the limit of proportionality (defined by a 0.1% ε offset) defined the linear region. The Poisson's ratio was nominally constant over the 400 N load range tested. Mean and standard deviations of the values for the transversely isotropic material properties were determined (Table 1) as well as the conversion to orthotropic constants used in the subsequent FE models to represent transverse isotropy (Table 1). Due to the fact that transverse isotropy is represented by only five independent material constants, calculation of G_{12} is based on $G_{12} = E_p/2(1+\nu_p)$ and ν_{23}, ν_{13} is based on $\nu_{23} = \nu_{13} = E_p \nu_{zp}/E_z$.

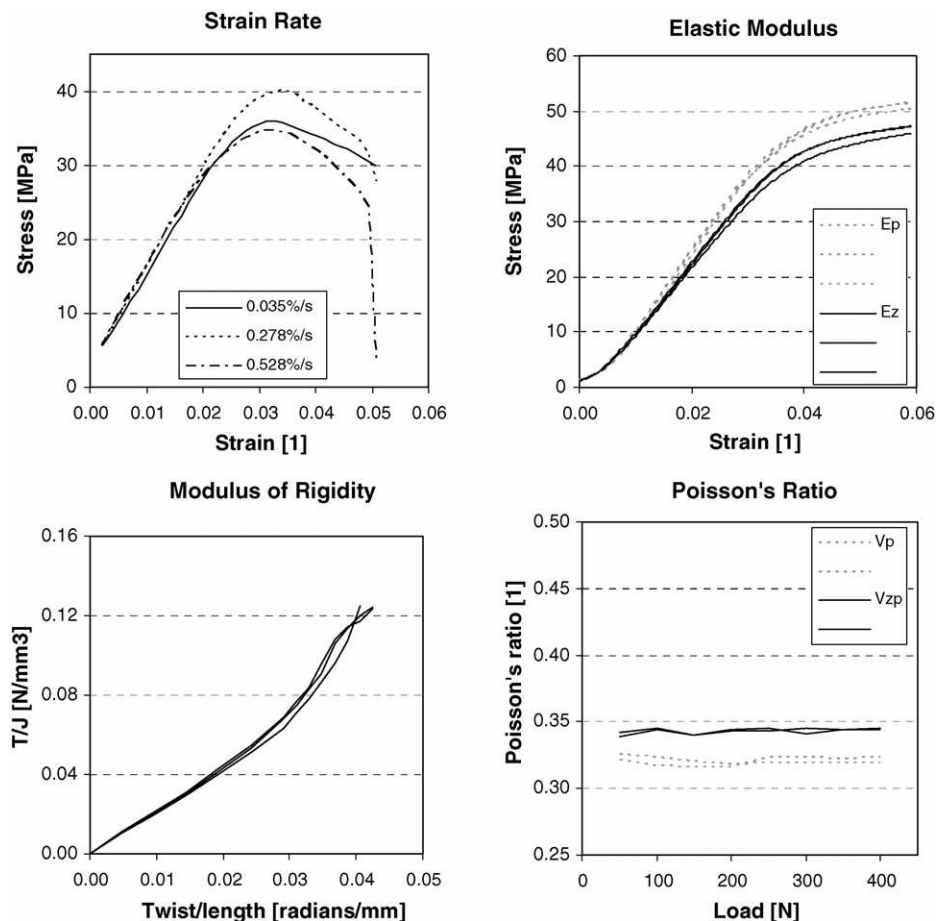


Fig. 3. Strain rate tests by uniaxial compression (top left), elastic moduli from uniaxial compression (top right), modulus of rigidity from a torsion test (bottom left) and the Poisson's ratio from a bending test (bottom right).

The FDM process accuracy based on comparison of caliper measurements of the prisms ($N=6$) with expected dimensions of $12.70 \text{ mm} \times 12.70 \text{ mm} \times 50.80 \text{ mm}$ was, respectively, 12.66 ± 0.05 , 12.72 ± 0.04 and $50.74 \pm 0.07 \text{ mm}$. Thus, the maximum relative error was 0.34%. The mean mass of the prisms was $7.77 \pm 0.02 \text{ g}$ and the volume was $8170.93 \pm 17.39 \text{ mm}^3$, therefore the density of the FDM material was determined to be $9.51 \times 10^{-4} \pm 9.93 \times 10^{-7} \text{ g/mm}^3$. This density value was used to determine the volume of the FDM models of the trabecular bone. The five FDM bone models had a mean mass of $48.30 \pm 0.03 \text{ g}$, and therefore represented a volume of $50,792 \pm 31.45 \text{ mm}^3$. Comparison of the physical volume of the FDM bone models with the stereolithography image volume ($50,845 \text{ mm}^3$) resulted in a 0.1% relative error. Comparison of the FDM bone replicas with the volume of the FE model ($51,378 \text{ mm}^3$) resulted in a 1.1% relative error.

The bending tests of the cantilever beams to estimate gauge mounting errors resulted in 0.79 ± 0.05 and $1.58 \pm 0.09 \text{ MPa}$ first principal stress on the rectangular and cylindrical beams, respectively, as measured by the gauges. The corresponding FE results for the same location were 0.76 ± 0.02 and $2.08 \pm 0.11 \text{ MPa}$, and analytical calculations based on an isotropic tissue modulus (1438 MPa) resulted in 0.74 and 2.22 MPa . Therefore, relative to the analytical solution, the difference in the gauge and FE results on the rectangular cantilever beam was 6.8% and 2.7%, respectively, and -28.8% and -6.3% for the cylindrical cantilever beam, respectively. The difference between gauge and analytical measurements on the rectangular cantilever beam is small (6.8% difference), likely due to a lack of curvature on the cantilever beam (a flat surface). On the cylindrical surface, the 1.58 MPa stress measured by the gauge is considerably less than the analytical result of 2.22 MPa (-28.8% difference). One factor that contributes to this difference is that the rosette surface coverage ranges up to 4 mm away (8 mm diameter) from the test point site (50 mm from the free end). The variations of surface stress within 4 mm, based on the FE model results, are as much as $\pm 6.6\%$ and -17.5% in the longitudinal and hoop directions, respectively. On the other hand, the analytical calculations serving as a benchmark are also limited due to the use of an isotropic modulus (in contrast to transversely isotropic), and the FE calculations are sensitive to their representation of a round cylindrical surface by brick elements which not only result in jagged surfaces, but can also lead to errors in the cylinder radius (stresses on surface

scale with the radius to a power of 3). Nevertheless, taking into consideration the limitations of each measurement technique, gauge measurement errors pose a problem due to their physical size. Therefore, for subsequent tests with the FDM bone replicas, smaller rosette gauges were used to minimize this error (0.79 mm active gauge length; $0.79 \text{ mm} \times 4.45 \text{ mm}$ overall coverage).

The five FDM bone replicas tested under uniaxial compression were used to calculate the mean and standard deviation of the apparent modulus, E_a ($343.43 \pm 13.24 \text{ MPa}$) as well as the first principal stress, σ_1 , at the flat ($3.00 \pm 0.60 \text{ MPa}$) and curved sites ($6.71 \pm 1.33 \text{ MPa}$) on the model surface (Table 2). A typical experimental result (Fig. 4) demonstrates a high degree of repeatability between measurements in a single specimen, and a linear apparent stress–strain relation in the 2% ϵ range tested. Local first principal stress was based on the mean sustained signal following application of the apparent-level 2% ϵ .

The newly developed orthotropic element-by-element FE solver was verified against the commercial FE solver for the small test model (slope = 1.00; intercept = $1.0\text{e}-5$; $R^2 = 1.0$). The four FE models representing uniaxial or axial compression with isotropic or orthotropic (transversely isotropic) properties were solved using the material constants determined experimentally (Table 1). The apparent stiffness and local first principal stress at the flat and curved surface sites were determined, and the comparison of those four model results with the experimental results are presented (Table 3). Based on the apparent stiffness, the uniaxial transversely isotropic FE model provided the best representation of the experimental results. The relative error between the FE and experimental results for apparent level stiffness was 0.62%, and for local stresses were 7.33% and 49.63% for the flat and curved surfaces, respectively.

4. Discussion

A validation approach based on complex bone geometries has been developed and tested. It was found that apparent-level stiffness could be predicted within 1% by the large-scale FE model, and the local level tissue stresses accuracy depended on the particular geometry of the tissue surface. Although the approach of generating augmented scaled replicas of trabecular bone from micro-CT data has been previously reported [25], to our knowledge this is the first time

Table 2

The apparent-level elastic modulus (E_a) and the first principal stress at the flat ($\sigma_{1,\text{flat}}$) and curved ($\sigma_{1,\text{curved}}$) rapid prototype replicas subjected to uniaxial compression for each of the five replicas tested

	Model					Mean	S.D.	CV (%)
	1	2	3	4	5			
E_a (MPa)	351.34	350.27	351.10	344.07	320.34	343.43	13.24	3.86
$\sigma_{1,\text{flat}}$ (MPa)	3.80	3.11	3.23	2.61	2.25	3.00	0.60	19.94
$\sigma_{1,\text{curved}}$ (MPa)	8.05	8.01	6.69	5.17	5.63	6.71	1.33	19.76

The mean, standard deviation (S.D.) and coefficient of variation (CV) for the five tests are presented.

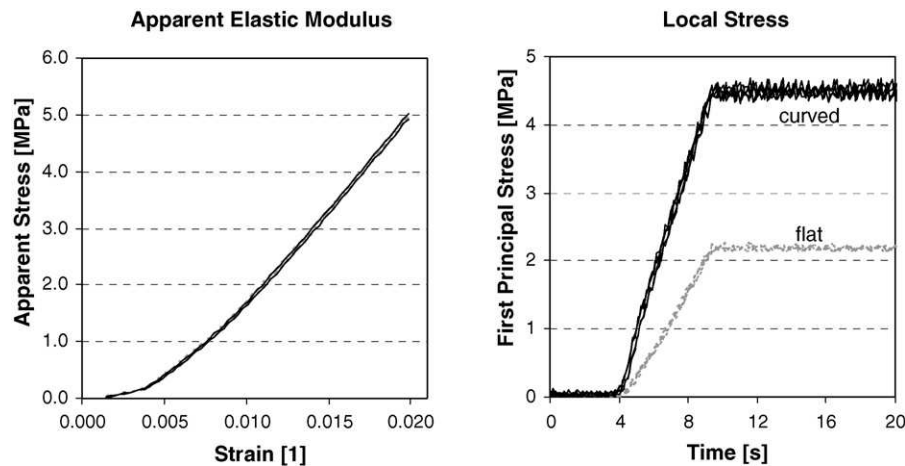


Fig. 4. An example test result (replica #4) from five consecutive uniaxial compressions demonstrating the consistency between tests. Five curves show the linear stress–strain relation for the apparent test results (left), and five curves each show the first principal stress before, during and after sustained loading (right) was applied between four and eight seconds for both the curved surface (top) and flat surface (bottom).

replicas have been used for a rigorous validation of the large-scale FE approach, and represents the first time a non-isotropic material property definition has been modeled in the solver. The approach is unique in that it represents the complex architecture of trabecular bone for bone-specific validation, and the experimental test results can be used for validation of future FE modeling methods as they develop.

The validation approach presented based on rapid prototype replicas focuses on the geometric issues related to large-scale finite element modeling, and not the ability to incorporate the bone tissue material properties into the model. To date, the standard approach to large-scale FE models is to assume that tissue modulus is constant throughout [10,16,39,40], thus homogeneous linear isotropic moduli are normally incorporated. It is known that trabecular tissue is neither homogeneous nor isotropic [41,42], but there is a lack of precise information about the spatial variability of tissue modulus that precludes the ability of including this information in large-scale FE models. Indentation testing [41,42] or relating micro-CT attenuation to tissue modulus [43] can provide an estimate of spatial variability, however these approaches are limited due to either the labour intensity, or problems with partial volume effects or beam hardening, respectively. Ultimately, even if the data were available, the

validation of models including more complex tissue properties would be challenging, and therefore the validation approach presented here focuses on the geometric aspects of large-scale FE modeling, and can be tailored to any bone type with varying geometries.

The ability of the rapid prototype replicas to serve as a validation tool for the large-scale FE method depends on the accurate characterization of the FDM material, and subsequent incorporation of those material properties into the FE model. The modified element-by-element approach was developed for this purpose to include nominally orthotropic tissue modulus, and its results were compared to a commercial implementation to verify numerical accuracy. Subsequently, the transversely isotropic properties of the FDM material could be incorporated into the FE model, and using boundary conditions that matched the physical experiment, there was less than 1% difference in the calculated apparent stiffness. Contrasting the results of the FE model with transversely isotropic or isotropic material properties, and axial or uniaxial boundary conditions confirmed that the best apparent-level results could be achieved with transversely isotropic materials and uniaxial boundary conditions. Matching the volume of the FE model and the replicas is important as tissue volume fraction plays an important role in the pre-

Table 3

The apparent elastic modulus (E_a) and the first principal stress at the flat ($\sigma_{1,flat}$) and curved ($\sigma_{1,curved}$) surfaces of the rapid prototype replica subjected to uniaxial compression

	Experiment	FE models			
		Orthotropic		Isotropic	
		Uniaxial	Axial	Uniaxial	Axial
E_a (MPa)	343.43 (13.24)	345.56 (–)	358.32 (–)	301.96 (–)	310.60 (–)
$\sigma_{1,flat}$ (MPa)	3.00 (0.60)	2.78 (1.39)	3.14 (1.44)	2.53 (1.32)	2.63 (1.36)
$\sigma_{1,curved}$ (MPa)	6.71 (1.33)	3.38 (1.30)	3.19 (1.28)	2.28 (0.76)	2.15 (0.73)

The experimental results are compared to the finite element models where the four models had either orthotropic (transversely isotropic) or isotropic material properties, and either uniaxial or axial compression boundary conditions. The standard deviation of the measurements are presented in brackets where available.

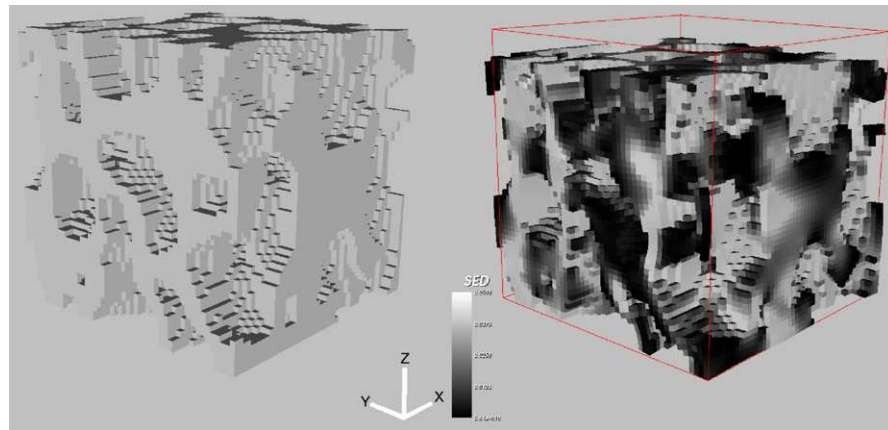


Fig. 5. The hexahedron-based finite element mesh generated directly from the micro-computed tomography data (left). Solution of the transversely isotropic uniaxial compression finite element model results in calculations of the six stress and six strain components, as well as the deformation due to loading. For simplicity, the strain energy density (SED) output was superimposed on the deformed mesh (scaled $10\times$ to exaggerate deformation) as per the loading conditions (right).

diction of bone strength [44,45], and the slightly higher tissue volume ($>0.1\%$) of the large-scale FE model may partially explain the corresponding higher predicted apparent modulus (1%).

The ability of large-scale FE models to accurately predict experimentally determined apparent-level bone specimen properties has been demonstrated previously, however those studies typically back-calculated a tissue modulus that provided the best fit between model and experiment [10,16,39,40,46]. Back-calculation inherently takes into account the effect of stress raisers due to the hexahedron mesh and effectively smoothes them—an approach that will not be possible in clinical patient-specific testing. In this work, the FDM material properties were determined independently by material testing, therefore it was encouraging that the hexahedron-based FE approach could be used in a “forward” approach to predict apparent-level mechanical properties to less than 1% .

The principal stress on the model surface varied as a function of the particular type of surface geometry on which it was measured, and differences on the flat surface were less (7%) compared to the curved surface (49%). The relatively larger difference on the curved surface was expected due to the limitation of hexahedron elements to represent curved surfaces [18]; however, the absolute magnitudes were likely influenced by inherent errors in the gauge measurements. A limitation of the rosette gauges for measurement of localized stress is that they cover a substantial region of the model which can influence their accuracy as was implied by the cantilever tests. Ideally, surface stresses should be measured at a finite focal point, and a possible experimental method to closer meet this goal could be a photoelastic stress analysis [47]. Nevertheless, while an absolute measurement of errors is limited, the gauge measurements were able to detect relatively large discrepancies on the curved surface, and a component of this error is likely related to use of brick elements in the FE analysis (i.e., stress raisers).

Patterns of oscillating errors were not evident on the model surfaces (Fig. 5), so accounting for the limitations of a hexahedron model by simply averaging results from neighbouring elements, particularly since the errors are unlikely stochastic, may not be the optimum approach. Alternatively, stress raisers could be reduced through improved FE meshing and solution strategies (i.e., large-scale FE methods for higher order or alternative elements) which is a current direction of our research group [22]. The experimental surface stress data from testing the replicas can be used for assessing these developments. Although the validation technique is limited to a small number of spatial locations on a model (due to practical limitations of the strain gauge technique), those limited validation points can provide important insight.

In conclusion, the validation approach used here uses a new orthotropic large-scale FE solver, micro-CT and rapid prototyping for architecture-specific validation. As new FE solution methods evolve, it will be critical to validate the apparent level and tissue-level mechanics which are increasingly being used, respectively, for non-invasive prediction of bone mechanical properties, and a basis for mechanically driven physiological models of bone adaptation.

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